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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,328	12/09/2004	Jeffrey A Smith	00789-05	7405

34444 7590 12/14/2007

UNIVERSITY OF VIRGINIA PATENT FOUNDATION
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CHARLOTTESVILLE, VA 22902

EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
12/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,328	SMITH ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-28,32,39-47 and 51-53* is/are pending in the application.

4a) Of the above claim(s) *10-20 and 39-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-28,32 and 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/11/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 9/21/2007 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1-9, 33-38 and 48-50 have been canceled.

2. Claims 10-20 and 39-47 have been withdrawn.

3. Remarks drawn to rejections under 35 USC 112, first paragraph and 103(a).

Claims 10-28, 32, 39-47 and 51-53 are pending in the case. Claims 21-28, 32 and 51-53 are currently under examination.

In the 103(a) rejection of record in the Office Action mailed 04/19/2007, claim 28 was inadvertently omitted from the rejection. It is included in the rejection below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 21-28 and 32 under 35 U.S.C. 112, first paragraph, because the specification while being enabling for the treatment of prostate and breast cancer using the compound of formula (III) and antisense oligonucleotides and interfering oligonucleotides, does not reasonably provide enablement for the treatment of all other types of cancers using the compound of formula (III) and the treatment of cancers using any other Rsk specific inhibitor, has been overcome by filing of an affidavit under 37 CFR 1.132, which shows test results for several other cancer cell lines. Enablement for the treatment of all cancers using the active agents as instantly claimed is seen.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of Claims 21-28, 32 and 51-53 under 35 U.S.C. 103(a) as being unpatentable over Matthes et al (Phytochemistry, 1980, 19, 2643-2650) in view of Bjorbaek et al (WO 00/66721), Marks et al (US 5,910,583), Kuijpers et al (US 5,733,523) and Pienta et al (Anticancer Research, 1994, 14, 2617-2620) and the rejection of Claims 25-27 under 35 U.S.C. 103(a) as being unpatentable over Bjorbaek et al (WO 00/66721) in view of Marks et al (US 5,910,583) and Kuijpers et al (US 5,733,523) are both being maintained for reasons of record.

Applicants have traversed the rejections arguing that:

1. The rejection assumes that it was known in the prior art that excessive Rsk activity is connected to cancer. Applicants were the first to correlate Rsk activity with cancer.

2. Matthes teaches that compound was slightly cytotoxic. This teaches away from the use of compound 7 for treating cancer. Matthes does not provide evidence that compound 7 is an Rsk-specific inhibitor nor that Rsk inhibition stops growth of tumor.

3. Applicants point out to additional studies published later by National Cancer Institute and the publication by Dai et al (Natural Product Letters, 1997, 10, 115-118; citation A in IDS of 9/21/2007) which teach that compound 7 of Matthes, which is also called 3',4'-O-deacetylafzelin has no antitumor activity..

4. Bjorbaek does not provide any data regarding regulation of Rsk activity and does not suggest treatment for cancer. Bjorbaek has addressed only Rsk2 and not other Rsk's.

5. Kuijpers discloses radioactively labeled oligonucleotides for use in radiation therapy. Kuijpers does not teach specific sequences for inhibiting activity directed against Rsk.

6. Marks also does not teach or suggest compositions comprising antisense oligonucleotides or methods of using them for treating cancer due to excessive Rsk activity.

7. Pienta teaches that genistein did not inhibit transplanted prostate tumor and hence there is no motivation to use such a drug.

Applicants' arguments are not found to be persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988 and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Regarding applicants' argument that they were the first to correlate the link between Rsk activity and cancer, the prior art teaches that the compound of their invention shows antineoplastic activity. Recognition of the mode of action does not lend a patentable distinction.

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69

USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); Abbott Labs v. Geneva Pharms., Inc., 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1310 (Fed.Cir.1999) ("If a product that is offered for sale inherently possesses each of the limitations of the claims, then the invention is on sale, whether or not the parties to the transaction recognize that the product possesses the claimed characteristics."); Atlas Powder Co. v. Ireco, Inc., 190 F.3d 1342, 1348-49 (Fed. Cir. 1999) ("Because sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention.... An inherent structure, composition, or function is not necessarily known.")>; SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a compound "inherently" anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound "inherently results in at least trace amounts of" the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate)

Matthes et al disclose a compound of structural formula 7, wherein two of the three hydroxyl groups on the sugar moiety are acetylated (page 2645). This compound is structurally same as the compound claimed in instant claims 21-24 and 52. Matthes teaches that the extract from the roots of Zingiber zerumbet (which contains compound 7 as an active agent) was tested against a rat neoplastic liver cell strain and found to be cytotoxic (page 2643, left column, Introduction, second and third paragraph). Even though Matthes does not mention that his compound 7 is an Rsk specific inhibitor as instantly claimed, his compound 7, which has the structural core as instantly claimed is one of the active agents in the extract of Zingiber zerumbet that shows cytotoxicity to neoplastic cells (cancer). Applicants documentation provided in support of their arguments (Dai and NCI references) do not show that Rsk activity is not involved in the cancer cell line used by Matthes. Dai has mentioned that the afzelins (same compounds as instantly claimed) were inactive in bioassay guided fractionation used in isolation

and characterization of active agents. Dai discloses the cytotoxicity of only Zerumbone (a structurally different compound) in the 60-cell line antitumor screen. The inactivity of the afzelins is not reported based on the antitumor screen using the same cell lines. Hence, the Dai and NCI references are not seen as enabling documents to overcome the rejection.

Bjoebaek et al teach inhibition of Rsk activity using nucleic acid construct expressing Rsk2 or a biologically active fragment thereof (page 2, line 26 through page 4, line 3; page 21, lines 1-7; example at pages 24 through 31). This means that nucleic acid constructs can be used for Rsk regulation. One of skill in the art would want to look at what else can be achieved by such regulation and one such extension would be with regard to cancer since nucleic acid and related oligonucleotides are known to be used for treatment of cancer.

Kuijpers et al teach in general the use of antisense oligonucleotides and their pharmaceutical formulations for the treatment of tumors (see abstract, col. 1, lines 26-40) and Marks teaches in general a variety of uses for oligonucleotide formulations including treatment of tumors (col. 5, lines 9-25).

The teachings of Bjobaek, Kuijpers and Marks suggest that nucleic acids and/or nucleotides can be used for treatment of cancer based on Rsk regulation even though such may not be exemplified or directly suggested. Pienta's teaching also suggests the use of the instant compounds for the treatment of cancer since Pienta's compound is structurally very close to the instant compounds. Similarity in structure and function entails motivation.

Based on the teachings of the prior art above one of ordinary skill in the art will recognize that:

1. Nucleic acid constructs can be used to inhibit Rsk activity and antisense-oligonucleotides have been used for treatment of cancer. Hence antisense-oligonucleotides and interfering oligonucleotides can be used for treating cancer based on regulation of Rsk activity. This suggestion is seen in the prior art.

2. Flavonoid glycoside of Matthes exhibits antineoplastic activity and like oligonucleotides may be used for inhibiting Rsk activity and hence inhibition of cell proliferation (cancer).

One of skill in the art would be motivated to use compounds of the type taught by Matthes since Pienta teaches that flavone compounds (compounds that are structurally similar to the compound of Matthes and instant compound III) have anticancer properties (page 2617, left column, first two paragraphs). One of skill in the art would look for closely related compounds that are more potent.

Obviousness based on similarity of structure and function entails motivation to make and use the claimed compound in expectation that compounds similar in structure will have similar properties. Where prior art compound essentially brackets the claimed compounds and are well known anticancer/antitumor agents, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new anticancer/antitumor agents. In re Payne, 606 F. 2d 303, 203, USPQ, 245, 254-55 (C.C.P.A. 1979).

Conclusion

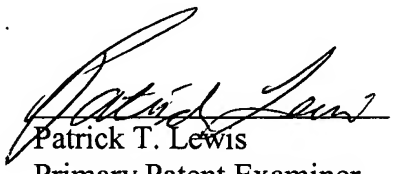
Claims 21-28, 32 and 51-53 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK



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